

Please cancel claims Claims 1 - 15, and add the following new claims:

16. A method of polymerizing aminoacid-N-carboxyanhydride monomers having a ring with a O-C₅ and a O-C₂ anhydride bond comprising:

(a) combining a first NCA monomer with an initiator molecule complex comprised of:

(i) a low valent metal capable of undergoing an oxidative addition reaction wherein the oxidative addition reaction formally increases the oxidation state by two electrons; and

(ii) an electron donor comprising a Lewis base;

(b) allowing the initiator molecule to:

(i) open the ring of the first NCA through oxidative addition across either the O-C₅ or O-C₂ anhydride bond;

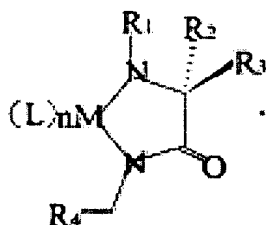
(ii) combine with a second NCA monomer, to form an amido-containing metallacycle; and

(c) allowing a third NCA monomer to combine with the amido containing metallacycle so that:

(i) the amido nitrogen of the amido containing metallacycle attacks the carbonyl carbon of the NCA and the NCA is added to the polyaminoacid chain; and

(ii) the amido containing metallacycle is regenerated. ✓

17. The method of claim 16 wherein the amido containing metallacycle is of the general formula:



wherein M is the low valent transition metal;

L is the Lewis Base ligand;

R1, R2 and R3 comprises a side chain of an amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine; and

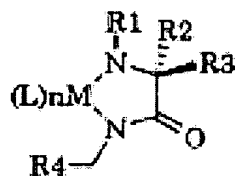
R4 is the polyaminoacid chain.

18. The method of claim 16 wherein the efficiency of the initiator is controlled by allowing the reaction to proceed in a solvent selected for its ability to influence the reaction.

19. The method of claim 17 wherein the solvent is selected from the group consisting of ethyl acetate, toluene, dioxane, acetonitrile, THF and DMF.

20. The method of claim 16, wherein the α -aminoacid-N-carboxyanhydride monomer is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine.

21. A five membered amido-containing metallacycle comprising a molecule of the general formula:



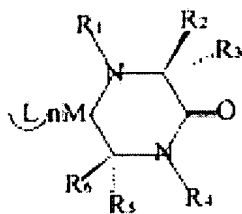
wherein M is a low valent transition metal;

L is a Lewis Base ligand;

R1, R2 and R3 comprises a side chain of an amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine; and

R4 is a hydrogen moiety or a polyaminoacid chain.

22. A six membered amido-containing metallacycle comprising a molecule of the general formula:



wherein M is a low valent transition metal;

L is a Lewis Base ligand;

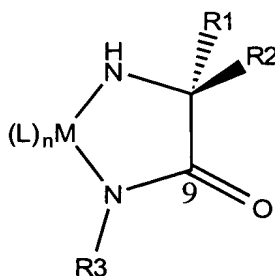
R1, R2, R3, R5 and R6 is a side chain of an amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine; and

R4 is a polyaminoacid chain.

23. The composition of claim 21 wherein the metal is a transition metal selected from the group consisting of nickel, palladium, platinum, cobalt, rhodium, iridium and iron.

24. The composition of claim 21 wherein the Lewis Base ligand is selected from the group consisting of pyridyl ligands, diimine ligands, bisoxazoline ligands, alkyl phosphine ligands, aryl phosphine ligands, tertiary amine ligands, isocyanide ligands and cyanide ligands.

25. A five membered amido-containing metallacycle comprising a molecule of the general formula:



wherein M is a low valent transition metal;

L is a Lewis Base ligand;

one of R1 and R2 is an amino acid side group and the other is hydrogen; and R3 is any functional end group capable of being attached to a primary amine group.

26. The amido-containing metallacycle of claim 25, wherein R1 or R2 comprises a side chain of an amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine.

27. The amido-containing metallacycle of claim 25, wherein R1 or R2 comprises a side chain of an amino acid selected from the group consisting of oligo(ethyleneglycol) functionalized (EG-)cysteine, EG-lysine, EG-serine, and EG-tyrosine.

28. The amido-containing metallacycle of claim 25, wherein R3 is a peptide, oligosaccharide, oligonucleotide, fluorescent molecule, polymer chain, small molecule therapeutic, or chemical linker that couples the polypeptide to another molecule.

29. A method of making an amphiphilic block copolypeptide, comprising the steps of: (1) generating a soluble block polypeptide by combining an amount of an oligo (ethyleneglycol) functionalized aminoacid-N-carboxyanhydride (EG-aa-NCA) monomer with an initiator molecule; and (2) attaching an insoluble block by combining the soluble block with a composition comprising at least one other amino acid NCA monomer.

30. The method of claim 29, wherein the amino acid component of the EG-aa-NCA monomer is lysine, serine, cysteine, or tyrosine.

31. The method of 29 wherein the insoluble block contains a mixture of amino acids.

32. A method of adding an aminoacid-N-carboxyanhydride (NCA) monomer to a soluble block polypeptide, comprising combining the NCA monomer with the soluble block polypeptide, said soluble block having one or more oligo(ethyleneglycol)-functionalized amino acid residues, so that the NCA monomer is added to the polypeptide.

33. A polypeptide composition comprising a block copolypeptide having:
- (a) a total number of overall monomer units that is greater than about 100 amino acid residues; and
 - (b) a distribution of chain-lengths of at least about $1.01 < M_w/M_n < 1.25$.
34. The block copolypeptide of claim 33, wherein said polypeptide has a number of overall monomer units that are greater than about 250 amino acid residues.
35. The block copolypeptide of claim 33, wherein said polypeptide comprises a least 3 blocks of consecutive identical amino acid monomer units.
36. The block copolypeptide of claim 33, wherein at least one of the blocks is components γ -benzyl-L-glutamate.
37. The block copolypeptide of claim 33, wherein at least one of the blocks is components ϵ -carbobenzyloxy-L-lysine.
38. The block copolypeptide of claim 33, wherein said polypeptide is composed of amino acid components γ -benzyl-L-glutamate and ϵ -carbobenzyloxy-L-lysine.
39. The block copolypeptide of claim 33, wherein said polypeptide is selected from the group consisting of a poly(ϵ -benzyloxycarbonyl-L-Lysine-*block*- γ -benzyl-L-glutamate), PZLL-b-PBLG, diblock copolymer and a poly(γ -benzyl-L-glutamate-*block*- ϵ -benzyloxycarbonyl-L-Lysine-*block*- γ -benzyl-L-glutamate) triblock copolymer.
40. An amphiphilic block copolypeptide comprising a soluble block polypeptide having one or more oligo(ethyleneglycol)-conjugated amino acid residues and an insoluble block comprised substantially of nonionic amino acid residues.
41. An amphiphilic block copolypeptide comprising: (1) a soluble block polypeptide having EG-lysine residues, and (2) an insoluble block polypeptide containing a mixture of two to three different kinds of amino acid components in a statistically random sequence.

42. An amphiphilic block copolypeptide consisting of at least 3 blocks, wherein one or more of the blocks is a soluble block polypeptide and another block is an insoluble block polypeptide.

43. An amphiphilic block copolypeptide comprising a soluble block polypeptide and an insoluble block polypeptide, said soluble block having at least about 30% mole percent identical amino acid residues having charged or oligo(ethylene glycol)-conjugated side chains and said insoluble block comprising at about 60 to 100 mole percent nonionic amino acid residues.

44. The amphiphilic block copolypeptide of claim 43 wherein the insoluble block comprises about 3 to about 60 mole percent of the total copolypeptide.

45. The amphiphilic block copolypeptide of claim 43 wherein the nonionic amino acid residues are selected from the group consisting of phenylalanine, leucine, valine, isoleucine, alanine and methionine.

46. The amphiphilic block copolypeptide of claim 43 wherein the amino acid residues having charged side chains are selected from the group consisting of glutamic acid, aspartic acid, arginine, histidine, lysine, and ornithine.

47. The amphiphilic block copolypeptide of claim 43 wherein the amino acid residues having oligo(ethylene glycol)-conjugated side chains are selected from the group consisting of EG-cysteine, EG-lysine, EG-serine, and EG-tyrosine.

48. A chain-end functionalized block polypeptide having ten or more consecutive identical amino acid residues and an endgroup selected from the group consisting of an oligosaccharide, oligonucleotide, fluorescent molecule, polymer chain, small molecule therapeutic, or reactive chemical linker to attach the block copolypeptide to another molecule.

49. A chain-end functionalized block copolypeptide having an end group selected from the group consisting of a naphthyl group, an alkyl group, an allyl group, and cysteinamide.

50. A polyaminoacid chain comprising at least ten consecutive oligo(ethylene glycol)-conjugated amino acid residues.

51. A method of forming vesicles comprising the step of suspending the amphiphilic block copolypeptides of claim 40 in an aqueous solution so that the copolypeptides spontaneously self assemble into vesicles.

52. The method of claim 51, further comprising the step of sonicating the suspended vesicles to form smaller vesicles having a diameter of about 50 nm to about 500 nm.

53. Vesicle-containing compositions comprising the amphiphilic block copolypeptides of Claim 40 and water.

54. A method for making EG-functionalized amino acid monomers, comprising the step of combining an ethyleneglycol (EG) derivative with an amino acid having a reactive side group.

55. The method of claim 54, wherein the EG derivative has the general formula $(\text{CH}_3\text{OCH}_2\text{CH}_2)_n\text{X}$; wherein n is about 1 to 3, and X is a reactive group selected from the group consisting of chloroformate, N-hydroxysuccinimide acetate, and halide.

56. The method of claim 54, wherein the amino acid is selected from the group consisting of lysine, serine, cysteine, and tyrosine.

57. The method of claim 54, further comprising the step of converting the EG functionalized amino acid to an NCA monomer.

58. A method of making a soluble block polypeptide comprising the step of combining an amount of an EG functionalized amino acid-N-carboxyanhydride (NCA) monomer with an initiator molecule comprising a low valent transition metal-Lewis Base ligand complex so that an EG functionalized polyamino acid chain is generated.

59. The method of claim 58 wherein the low valent transition metal is selected from the group consisting of nickel, palladium, platinum, cobalt, rhodium, iridium and iron.

60. The method of claim 58 wherein the Lewis Base ligand is selected from the group consisting of pyridyl ligands, diimine ligands, bisoxazoline ligands, alkyl phosphine ligands, aryl phosphine ligands, tertiary amine ligands, isocyanide ligands and cyanide ligands.

61. The method of claim 58 wherein the EG functionalized-amino acid-N-carboxyanhydride monomer is selected from the group consisting of EG-cysteine, EG-lysine, EG-serine, and EG-tyrosine.

62. A method of preparing a polypeptide having a defined end group comprising the steps of:

- a) combining an alloc-amino acid amide with an initiator comprising a low valent transition metal-Lewis Base ligand complex for a time and under conditions effective to form an amido-amidate metallacycle; and
- b) adding one or more amino acid-N-carboxyanhydride monomers to the metallacycle for a time and under conditions effective to form a polypeptide having an end group derived from the alloc-amino acid amide.